Available online at www.sciencedirect.com

ScienceDirect

Procedia Technology 27 (2017) 39 – 41

Procedia Technology

Biosensors 2016

Ultra-low-light CMOS biosensor complements microfluidics to achieve portable diagnostics

Zhimin Ding, Cai Xu, Yifang Wang, Gianfranco Pellegrini*

Anitoa Systems, LLC, 149 Commonwealth Drive Suit 1001, Menlo Park, CA 94025, USA

Abstract

Innovations in ultra low-light CMOS bio-optical sensor design, combined with microfluidics technology can enable a new generation of low cost, portable molecular diagnostics platforms. This combination of technologies have been applied successfully in a miniaturized qPCR system, and a chemiluminescence microfluidic immunoassay platform to detect a variety of infectious pathogens. Cost reduction and miniaturization of molecular test enabled by this technology will have positive impact on global battle against infectious diseases.

Peer-review under responsibility of the organizing committee of Biosensors 2016

Keywords: CMOS biosensor; Microfluidics; Portable molecular diagnostics; qPCR; Chemiluminescence immunnoassay; Point-of-care; Bioinformatics.

1. Introduction

The outbreak of Ebola in West Africa two year ago underscores the urgent need for globally affordable tools to help fight infectious diseases. Among these, a method to rapidly and accurately identify the infectious pathogens and their drug-resistant variants on-site is of particular importance.

* Corresponding author. Tel.:+1-408-887-6026; fax: +1-650-813-9777.
E-mail address: zhimin.ding@anitoa.com

Peer-review under responsibility of the organizing committee of Biosensors 2016
doi:10.1016/j.protcy.2017.04.019

Researchers have tried many methods to achieve small, portable, and automated solutions to perform molecular test near patient or in the field. To this end, much effort has been put into developing novel microfluidic “lab-on-chip” technologies [1]. While microfluidic devices enable sample and diagnostic assay to interact on a small disposable chip-format device, these chips still need to be "read out" by instruments such as a fluorescence microscope to obtain the final test results. Due to small reaction volume and dense reaction sites on a microfluidic chip, the type of the instruments that has the capability to read out such reactions are usually bulky and expensive.

Microfluidic technology alone thus fell short of providing a complete solution for portable molecular diagnostics. We took a holistic approach by innovating on technologies that enable compact microfluidic read out instrumentation as part of the total solution. For this purpose, we introduce a CMOS bio-optical sensor that is ultra sensitive, highly integrated and low power. Based on fluorescence and chemiluminescence signalling principle, and combined with microfluidics technology, this CMOS biosensor can enable truly portable and affordable molecular diagnostic platforms.

2. Ultra-low-light CMOS Bio-optical sensor

We have fabricated a CMOS image sensor (CIS), called ULS24, on a 0.18 µm CIS technology from a leading commercial CMOS foundry. With a small die size of 4.8mm X 4.8mm, the chip has been shown to achieve 3e-6 lux detection sensitivity (narrow band @550nm), while consuming only 30mW. ULS24 is capable of detecting just a few molecules labelled with fluorescence reporter probes. This is sufficient to replace the bulkier and more expensive photon multipliers (PMTs) and cooled CCDs commonly found in many of today's molecular test instruments.

Due to its wide adoption in consumer digital cameras and smartphone cameras, CMOS image sensor technology have steadily improved over the years. Still more improvements in process, circuit, and software are needed to enable CMOS to match the sensitivity of PMT and cooled-CCDs. To meet this challenge, we adopt novel manufacturing process technology and circuit design techniques to reduce the noise inherent in CMOS image sensors active pixels to achieve a high signal-to-noise ratio (SnR). The excessive noise that cannot be eliminated in the chip due to limitations of physics is further filtered through a digital signal processing algorithm, called "Intelligent Dark-current Management" algorithm.

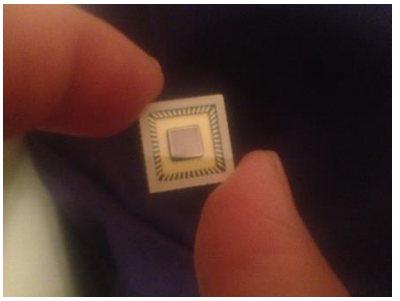

Figure 1, Anitoa's ULS24 ultra-low light CMOS Bio-optical sensor chip

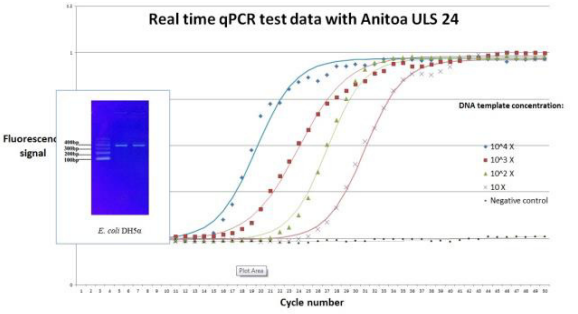

Figure 2, Anitoa ULS24 CMOS biosensor successfully applied in qPCR to detect E Coli. (DH5a), HBV (wild type and rtM2041), and foot-and-mouth disease (EV71 and CA16), with limit of detection as low as 4 copies per reaction.